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A Guide for Penicillin Treatment

PREPARED BY THE
MEDICAL ADVISORY COMMITTEE ON PENICILLIN*

CLINICAL USE OF PENICILLIN

I. Penicillin should be used in the treatment of the following conditions:

1. *Septicaemias* caused by *Staphylococcus aureus*, *Streptococcus haemolyticus* or *Pneumococci*.
2. *Meningitis* caused by *Staphylococcus aureus*, *Streptococcus haemolyticus* or *Pneumococci*, and cases of meningococcal meningitis not responding after two to three days of adequate sulphonamide therapy.
3. *Gas gangrene*.
4. *Serious infections* caused by *Staphylococcus aureus*, *Pneumococci*, *Streptococcus haemolyticus* and anaerobic streptococci, such as:
   (a) Acute osteomyelitis.
   (b) Cellulitis.
   (c) Puerperal sepsis.
   (d) Mastoiditis and otitis media.
   (e) Cavernous and lateral sinus thrombosis.
   (f) Staphylococcal and haemolytic streptococcal pneumonia.
   (g) Pneumococcal pneumonia not responding after three days of adequate sulphonamide therapy.
   (h) Empyema and suppurative arthritis.
   (i) Carbuncles and soft tissue abscesses.
5. *Gonococcal infections* causing arthritis, ophthalmia, endocarditis and epididymitis.

   NOTE: If supplies of penicillin permit, cases of gonorrhoea not responding to adequate sulphonamide therapy may be treated.

**Office of the Controller of Chemicals, Department of Munitions and Supply, 1235 McGill College Avenue, Montreal.*

II. Penicillin may be a useful and effective agent in the conditions listed below but further clinical investigation is necessary to define its value:

(a) Chronic osteomyelitis (before and after operation).
(b) Actinomycosis.
(c) Subacute bacterial endocarditis.
(d) Perforations of abdominal viscera and associated subphrenic, pelvic and other abscesses, if the predominant micro-organism is gram-positive.
(e) Syphilis.

NOTE: Although encouraging results have been obtained with penicillin in the treatment of syphilis, present supplies of penicillin do not warrant its use in the treatment of this condition, and distribution for this purpose cannot be approved.

III. Penicillin is of little or no value, and should not be used, in the treatment of the following conditions:

(a) All infections caused by viruses, such as: influenza, primary atypical pneumonia, encephalitis lethargica and anterior poliomyelitis.
(b) Tuberculosis.
(c) Typhoid fever, dysentery and cholera.
(d) Undulant fever and tularaemia.
(e) Rheumatic fever and rheumatoid arthritis.
(f) Infections in which the dominant organisms are gram-negative bacilli.
(g) Infectious mononucleosia.
(h) Hodgkin's disease, leukaemias and malignant disease.
(i) Ulcerative colitis.
(j) Meningitis and other conditions due to *Haemophilus influenzae* or *Bacillus of Friedlander.*
(k) Pemphigus.

Administration of Penicillin

Penicillin is supplied as a yellowish-brown powder in ampoules or vials containing 100,000 units each. To maintain the potency of the preparation the ampoules or vials must be stored at refrigerator temperature. The powder is freely soluble and may be dissolved in a small amount of distilled water, physiological saline, glucose-saline or glucose solution. When reconstituted as a solution most penicillin preparations are relatively unstable. It is advisable, therefore, to make up each day only enough solution to last for 24 hours or at most 48 hours, and to store the unused portion, under aseptic precautions, at refrigerator temperature. In preparing penicillin for systemic administration it is customary to dissolve the powder containing 100,000 units in 20-cc. sterile, pyrogen-free distilled water or sterile physiological saline to give a solution with 5,000 units per cc.

Either the intravenous or the intramuscular route may be used for the systemic administration of penicillin, but no matter which route is used penicillin is rapidly excreted in the urine. Following a single injection it is impossible to detect penicillin in the blood three to four hours later. In order to maintain an adequate blood concentration of penicillin it is necessary to repeat the injections every three to four hours or to give the penicillin as a continuous intravenous infusion.

Intravenous administration may be accomplished: (1) by injecting a dose every three hours, day and night, into the rubber tubing of a continuous

intravenous drip; (2) by mixing half the daily dose in 1 litre of infusion fluid (saline or glucose) and adjusting the flow of the intravenous drip to deliver this amount in twelve hours (30 to 40 drops per minute).

If the intramuscular route is used, the total volume of fluid injected should be small and contain 5,000 units of penicillin per cc. The injections should be repeated every two to four hours, day and night, depending on the severity of the infection.

Subcutaneous injections are not recommended since they are apt to be painful.

Dosage of Penicillin

The dosage of penicillin to be used in the treatment of a disease varies with the age and weight of the patient and with the type and severity of the infection. More experience with this new chemotherapeutic agent is required before any final decision in regard to dosage can be made. However, satisfactory results have followed the use of penicillin at the dosage outlined below, but it should be realized that modifications may have to be made for each individual case.

A. *Systemic Therapy:*

For *septicaemias* and other severe infections in adults it is recommended that the daily dose be 120,000 units until the temperature returns to normal and the condition of the patient is satisfactory. It is possible that a larger daily dose may be required for fulminating infection.

In contrast to the severe infections, which require on the average 1,000,000 units of penicillin, uncomplicated cases of gonococcal urethritis respond well to 100,000 units of penicillin given intramuscularly in doses of 10,000 units every three hours. However, cases of gonorrhoea with complications, such as arthritis, may require the same daily dose as a severe infection.

In cases of *meningitis*, in addition to systemic therapy, it is necessary to inject penicillin into the subarachnoid or cisternal space because diffusion of penicillin from the blood into the cerebrospinal fluid does not occur in appreciable amounts. Following removal of cerebrospinal fluid, it is recommended that 10 cc. of a penicillin solution containing 1,000 units per cc. in physiological saline be injected intrathecally each day until the signs and symptoms of meningitis have subsided.

In *infected effusions*, 50,000 units of penicillin in 50 to 100 cc. of physiological saline should be injected into the pleural cavity every 48 hours following the aspiration of the pus or fluid. After four doses the effusion usually remains sterile and may be absorbed following subsequent aspirations. In other cases drainage is necessary because the pus becomes too thick to be aspirated or infection recurs.

B. *Topical Application:*

Penicillin solutions containing 250 to 500 units per cc. may be instilled into infected sinuses or applied locally. Such solutions should not be used as irrigating fluids since several hours of contact of penicillin are necessary before its full effect on susceptible bacteria is exerted.

Puerperal Infection due to Haemolytic Streptococcus Group A (Type 14)

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ON June 4, 1944, the Department of Health of Ontario was informed that obstetrical patients were developing fever in the maternity unit of a general hospital in Ontario. During the months previous to the investigation, the maternity unit of this hospital had had as many as forty patients at one time, with a monthly average of one hundred. As fever had been noticed among patients for some time, the case histories of all the maternity cases from January 1 to June 15, 1944, were examined. Patients showing a temperature of 100.4° F. or over for two consecutive days were considered abnormal.

TABLE I

PUERPERAL SEPSIS IN THE MATERNITY UNIT OF A GENERAL HOSPITAL
Number and percentage of patients showing an abnormal puerperium (Temperature 100.4° F. for 2 consecutive days), January-June, 1944

Month	Total Patients	Patients with normal puerperium	Patients with abnormal puerperium	
			Number	Per cent of Total
January	104	64	40	38.4
February	92	47	45	48.9
March	96	54	42	43.7
April	89	59	30	33.7
May	100	59	41	41.0
June	21	15	6	28.6
Total	502	298	204	40.6

Table I shows the number and percentage of patients with a morbid puerperium for the six-months' period. During this time, 502 patients were admitted, and 40.6 per cent showed abnormal fever. In February 48.9 per cent of the patients were ill.

The day on which the fever began is shown in Table II. In 58 per cent the fever appeared on the third and fourth days after delivery.

The duration of fever in the morbid cases in the different months is shown in Table III. After the first day, sulpha drugs were given to many cases. This would tend to shorten the duration of the fever. Even with the use of sulphonamides, 16.5 per cent of the patients had fever for more than 6 days.

TABLE II

PUERPERAL SEPSIS IN THE MATERNITY UNIT OF A GENERAL HOSPITAL
Number of days after delivery that fever first occurred in 204 patients

Month	Day fever appeared										
	1st	2nd	3rd	4th	5th	6th	7th	8th	9th	10th	11th
January		5	15	14	5		1				
February	3	13	14	10	2	2				1	
March	1	9	13	11	1	3	2	1	1		
April		4	9	10	2	2	1			1	1
May	2	5	11	8	5	4	2	1		3	
June			2	2		1	1				
Total	6	36	64	55	15	12	7	2	1	5	1
Per cent	3.	18.	31.2	26.8	7.4	6.	3.8	.8	.4	2.2	.4

TABLE III

PUERPERAL SEPSIS IN THE MATERNITY UNIT OF A GENERAL HOSPITAL
Duration of fever, in days, of 204 patients with morbid puerperium

Month	Duration of fever in days														
	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
January	4	14	6	5	2	3	4	1						1	
February	11	10	9	4	5	2	3	1							
March	6	6	11	10	3	2	2				1	1			
April	9	3	5	4	4	3	1		1						
May	8	9	3	5	10	1	1	1	1			1			1
June	1	2	1	1					1						
Total	39	44	35	29	24	11	11	3	3		1	2		1	1
Per cent	19.1	21.5	17.	14.1	11.8	5.5	5.5	1.5	1.5		.5	1.0		.5	.5

TABLE IV

PUERPERAL SEPSIS IN THE MATERNITY UNIT OF A GENERAL HOSPITAL
Haemolytic streptococcus on perineal pads and fever in the puerperium in 38 mothers

Organism isolated on perineal pads	Haem. Strep. Pos. Fever Pos.	Haem. Strep. Pos. Fever Neg.	Haem. Strep. Neg. Fever Pos.	Haem. Strep. Neg. Fever Neg.
Haemolytic Strep. Group A—Type 14	20	4	2	10
Haemolytic Strep. Group B	0	2	0	0

Perineal pads from 38 mothers were examined for organisms. Haemolytic streptococci were isolated from the pads of 26 patients. The results are seen

in Table IV. Twenty patients with fever showed haemolytic streptococcus Type 14. In six mothers without fever, haemolytic streptococcus was isolated. Four of these were Type 14 and two were Group B. Two patients had fever but no haemolytic streptococci were isolated. One of these cases had an adherent placenta. Ten patients had no fever and no haemolytic streptococci were isolated.

TABLE V

PUERPERAL SEPSIS IN THE MATERNITY UNIT OF A GENERAL HOSPITAL
Haemolytic streptococcus in the throats of Nurses and Maids in the Maternity Unit

	Haemolytic streptococcus				
	Absent	Present			
		Group A Type 14	Group B	Group C	Group F
Nurses	14	1	1	1	2
Maids	1	1			

The findings from throat swabs are shown in Table V. Eighteen nurses and two maids in the unit were examined. One nurse and one maid had type 14 haemolytic streptococci in the throat.

A throat swab from one mother who had type 14 on the perineal pad, failed to show haemolytic streptococcus. A culture from the husband's throat also failed to show haemolytic streptococcus. Throat swabs from the remaining mothers were not obtained.

FACTORS PREDISPOSING TO INFECTION

Conditions in the materity unit were not at all satisfactory and there were many factors which could have produced the puerperal infection in the mothers. A few of the most important faults are given below.

Sterilization of Supplies: There was only one autoclave in the hospital for the sterilization of surgical and obstetrical supplies. Materials were rushed through with inadequate sterilization. The operator timed the load for thirty minutes after the pressure gauge registered twenty pounds' pressure. There was no thermometer on the autoclave. It was found that, although the gauge registered 20 pounds, it took 20 minutes for the temperature at the outlet to reach 150 degrees F. Moreover, the vacuum was not working properly and bundles were often wet when removed from the autoclave.

Dry Sweeping: The labour room, halls and patients' rooms were swept with a dry broom. Building operations were in progress and there was a great deal of dust throughout the hospital.

Labour Room: Five maternity patients were crowded into one labour room and it was necessary to pass through this room to enter the delivery room. Husbands of mothers in labour were permitted to sit in the labour room.

Admitting Room: No admitting room was provided and the patients were admitted to the labour room in their street clothes.

Isolation: No isolation room for mothers was provided. Patients with an

abnormal puerperium were not isolated and isolation techniques were not observed.

Nursing Staff: There was inadequate nursing staff, especially on the night shift, to carry out the desired techniques.

Techniques: Techniques were faulty in many instances. The nurses did not wear masks when changing the perineal pads. Facilities for washing the hands in the patients' rooms were poor and as a result the hands were not always washed between the changing of pads. Individual bedpans were not always provided for each patient. T-binders were not used to keep the perineal pads in place.

Throat Swabs and Sterility Tests: Throat swabs from nurses were not taken regularly and cultured for the presence of the haemolytic streptococcus. Sterility tests on dressings and perineal pads were infrequently carried out.

Discussion

In 1942, 36 per cent of all the maternal deaths in the U.S.A. were due to infection, of which 17 per cent followed abortion. A number of the remaining 19 per cent of infections must have been puerperal sepsis. With the use of sulphonamide drugs there is a tendency to relax and to disregard the rigid techniques which are necessary to avoid the introduction and spread of puerperal infection in the maternity units.

During the war, the maternity units have been overcrowded. Nurses are difficult to obtain, as many have gone into more remunerative work. This lack of nursing staff makes it very difficult to see that proper techniques are followed. Internes are also at a premium in many hospitals. Swabs from nurses' throats are not taken at regular intervals, or as often as they should be.

It is quite possible that the use of the sulpha drugs cut short the fever in many of these cases. In two patients the organisms appeared to be sulphonamide-resistant and penicillin was required to effect a cure. Had it not been for the use of these drugs, some of the patients no doubt would have died of puerperal infection.

Summary

1. Haemolytic streptococcus Group A (Type 14) was the infecting organism in puerperal sepsis in the maternity unit of a general hospital. This organism was present on the perineal pads in 24 out of 38 mothers examined. Twenty of these patients had a morbid puerperium. The same organism was present in the throat of one nurse and one maid in the unit.

2. The infection was present for more than five months in the unit. Severe symptoms were prevented in many patients by the use of sulphonamide therapy. Two patients required penicillin.

3. There was overcrowding in the unit; the sterilization of supplies was inadequate; there were insufficient nurses available and the resulting techniques were poor; and throat swabs were examined from the nurses at irregular intervals.

The Group A strains of haemolytic streptococcus were typed by the Laboratory of Hygiene, Ottawa. This service is appreciated.

Statistical Estimation of Vitamin C Intake of Troops on Canadian Army Garrison Rations[1]

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THE intake of vitamin C by troops on army rations is determined by the ascorbic-acid content of the items served and their acceptability to the individual consumer. During the winter of 1941-42 two surveys were conducted to determine the individual daily intake of vitamin C from vegetable sources included in the regular issue of army garrison rations, by troops serving in the Base Post Office and the District Depot, M.D. 3, both in Ottawa. Estimates were deduced from chemical determinations of the vitamin C content of the vegetables, both fresh and cooked in various ways, and from statistics based on the amounts of vegetables actually consumed by individuals.

METHODS

Chemical

Representative samples of vegetables taken from each cooking-vessel at the time of serving were transported to the laboratory in ½-pint sealers and extracted within 1 hour. Thirty-five grams of fresh or cooked vegetables were placed in a Waring blendor together with 150 ml. of 2 per cent metephosphoric acid to which 1 ml. of 1 per cent KCN had been added, and blended for 5 minutes under an atmosphere of carbon dioxide. The resulting suspension was poured into 250-cc. centrifuge bottles to which were added a further 30 ml. of acid used to wash the blendor jar, and the combined volumes centrifuged at 2000 r.p.m. for 15 minutes. (Washing was dispensed with in the later experiments.) Twenty-five ml. of the supernatant liquid were pipetted off and titrated with 2:6 dichlorophenol indophenol (80 mg. in 250 ml. water) for the determination of l-ascorbic acid. For the determination of dehydro-ascorbic acid, a further volume was reduced with hydrogen sulphide, the excess sulphide being removed with a current of nitrogen.

The moisture content of all samples was determined, and allowance made for the diluting effect on the volume of the extract in computing the analytical results.

In the tables which follow, the analytical results are expressed as milligrams of total ascorbic acid (reduced plus dehydro) per 100 grams of the material sampled.

Statistical

Statistical estimates of vegetable consumption by individuals were arrived at through a combination of enumeration and random sampling processes.

[1]*Contribution from the Division of Applied Biology, National Research Laboratories. Issued as N.R.C. No. 1337.*

[2]*Statistician. Now on loan to the Royal Canadian Air Force.*
[3]*Biologist.* [4]*Laboratory assistant.*

In both units the men were served in cafeteria fashion, and the number taking none, one or both of the vegetables available at any particular meal was determined by direct enumeration. All vegetable kettles were weighed immediately before and after serving, and the average weight of the individual portion of each vegetable computed. In order to determine the variability of individual servings, 15-20 representative servings issued by the Base Post Office cook were weighed immediately before each meal. The relative variance of seven series of successive helpings examined in this way was found to be of the same order, corresponding to a standard deviation of $\pm$ 13 per cent. In practice this basic variation in successive servings was increased as some individuals demanded more or less than the amount originally given. In consequence, a standard deviation of $\pm$ 20 per cent was considered to be more representative of the actual variability of individual servings and this figure was used in all subsequent calculations.

After each meal, the proportion of individuals leaving any residue of either or both vegetables uneaten was determined by enumeration of a representative sample comprising about 100 men in the case of the Base Post Office unit and 150-200 in the case of the District Depot. Individual weights of a random selection of 25-50 vegetable residues were also secured on each occasion.

From the foregoing enumerations it was possible to estimate for each meal the proportion of individuals in the consumption categories listed in Tables II and VI. These categories together with the preceding information with respect to the average weight and variation of servings and uneaten residues, and the ascorbic acid content of the vegetables as served provided the data necessary for estimation of individual vitamin C intake.

The range of intake of individuals taking one vegetable only but consuming the entire amount given to them may be specified by a frequency curve deducible from the mean weight of vegetable served, the variance of individual portions, and the ascorbic acid content of the material as served. In a similar manner, a frequency curve specifying the amounts of ascorbic acid left unconsumed by individuals taking one vegetable only and failing to eat their entire serving may be deduced. From the estimated parameters of these frequency curves it was possible to estimate the parameters of the frequency curve specifying the range of intake of individuals consuming only part of an initial serving of one vegetable. An extension of this process was used to deduce frequency curves of estimated vitamin intake deduced for individuals in each of the consumption categories specified. Then by reference to tables of the appropriate probability integrals the level of ascorbic acid intake bounding successive deciles of the area under each curve was determined and the scale of intake of the individuals in each category estimated, the upper limit being defined by the 99.9 per cent point of the curve, i.e., the ascorbic acid level having a theoretical probability of only 1 in 1000 of being attained or exceeded. Finally, the results for all categories were combined to yield an estimate of the total proportion of men whose intake of vitamin C from the meal in question was from 0 to 5, 5 to 10, 10 to 15 milligrams, etc.

Results

Vitamin C Content of Raw and Cooked Vegetables

The results of chemical analyses of raw and cooked vegetables are summarized in Table I.

TABLE I

Vitamin C Content of Raw and Cooked Vegetables, expressed as mg. Total Ascorbic Acid per 100 g. of Material Sampled at the Base Post Office and the District Depot, M.D. 3, Ottawa

Vegetable	Uncooked (sampled from stores)	As served		Percentage loss	
		Base P.O.	Dist. Depot	Base P.O.	Dist. Depot
Potatoes, boiled	12	3	3	75	75
" mashed	12	2	2	83	83
" fried or roasted	12	2	2	83	83
Cabbage, boiled	47	11	..	77	..
" boiled + meat broth	..	3	5	94	89
Carrots, boiled	6	2	2	67	67
Coleslaw (cabbage, carrot, onion and vinegar)	..	..	36	..	..
Peas, canned, boiled	11	..	5	..	55
" " boiled, liquor from	13	..	..	..	..
Tomato, canned (served cold)	19	16	17	16	10
Turnips, boiled	44	7	1	84	98

In view of the time of year (February) at which observations were made, the vitamin C content of the samples taken from stores was commendably high in relation to the averages reported for fresh vegetables of the same species. It is also evident, however, that this originally high quality was largely dissipated by the cooking procedure then current and that the vitamin C content of all the cooked vegetables examined as served was low.

Vitamin C Intake of Base Post Office Troops

Observations were made in the Base Post Office mess for three days commencing February 10, 1942, attention being confined to the noon and evening meals in view of the negligible amount of vitamin C derivable from any of the breakfast items.* From the enumerations made on these occasions the statistics of consumption listed in Table II were deduced. The vegetables served

TABLE II

Percentage of Base Post Office Troops in Various Categories of Vegetable Consumption

Consumption category	February 10th		Feb. 11*	Feb.12 †
	Dinner	Supper	Dinner	Dinner
Took no vegetable	1½	½	..	½
Took potatoes only, ate entire serving	15	20	28	27
Took potatoes only, left some uneaten	3½	4½	10	4
Took second vegetable only, ate entire serving	1½	3	1	½
Took second vegetable only, left some uneaten	½	..	..	..
Took both vegetables, ate entire serving of both	36	48	14	25
Took both vegetables, ate all of second, left some potatoes	15	12	16	8
Took both vegetables, ate all potatoes, left some of second vegetable	11	2	6	17
Took both vegetables, left some of both	16	9	25	18
Took two servings of second vegetable	..	½	..	..
Took two servings of potatoes	..	..	..	..
Took two servings of both vegetables	..	½	..	..
Number of men enumerated	192	178	201	184

*Supper—beef stew; statistics not enumerated, for reasons given.
†Supper—roasted potatoes and cold canned tomatoes; statistics for February 10th used.

**Since this survey was made, grapefruit juice, tomato juice and fortified apple juice have been included in the regular issue.*

on each of these days, and the weight of average portions were as follows: February 10th, dinner: boiled potatoes (159 g.) and boiled carrots (109 g.); supper: roasted potatoes (148 g.) and cold canned tomatoes (76 g.); February 11th, dinner: boiled potatoes (140 g.) and boiled cabbage (88 g.); supper: beef stew with potatoes, cabbage and turnips; February 12th, dinner: mashed potatoes (292 g.), boiled potatoes (125 g.) and mashed turnips (129 g.); supper: roasted potatoes and cold canned tomatoes.

At dinner on February 10th, 36 per cent of the men ate an entire serving of both boiled potatoes and carrots; at supper 25 per cent took potatoes only, while 48 per cent of them consumed an entire serving of the two vegetables.

The boiled potatoes and cabbage offered at noon on February 11th were even less acceptable as only 14 per cent of those served were estimated to have eaten an entire serving of both vegetables. The vegetable constituents of supper on this date consisted of carrots and turnips unserved at previous meals and now included with potatoes in a beef stew. Detailed observations were not made for this meal as it can be assumed with confidence that the scale of vitamin C intake equivalent to that deduced for the day before would more than do justice to it.

Mashed potatoes served with turnips at dinner on February 12th appeared to be favoured by the men and were served more generously, the average serving being about double that for other forms of potato. At this rate of issuance the first 125 individuals exhausted the supply and the remainder of the 184 men enumerated received boiled potatoes. Again it was estimated that only 15 per cent of the men ate entire servings of both vegetables. As supper was a repetition of that served on February 10th, statistics for that day were applied again.

The average recorded weights of uneaten residues are shown in Table III. It will of course be realized that these figures imply not that, for example,

TABLE III

VEGETABLE RESIDUES LEFT UNEATEN BY BASE POST OFFICE TROOPS

Vegetable	Percentage of men		Average weight of serving, grams	Average weight of residue, grams	Average residue as per cent by weight of average serving
	Taking serving	Leaving residue			
Potatoes, boiled	96	43	159	64	40
Potatoes, roasted	96	26	148	54	36
Potatoes, mashed	99	30	292	46	16
Carrots, boiled	80	28	109	39	36
Cabbage, boiled	62	31	88	21	24
Turnips, boiled	68	35	129	48	37
Tomato, cold	75	11	76	11	14

37 per cent of the entire quantity of turnips served was uneaten, but that it is estimated that this was the average proportion left by the 35 per cent of individuals who accepted a serving and then failed to consume all of it. A tendency of some individuals to leave the vegetables virtually untouched was most pronounced in the case of potatoes, but was evident in all instances.

By means of the computational procedure perviously outlined, the scale of

estimated individual vitamin C intake shown in Table IV was deduced for the four meals surveyed. From these estimates of intake at each meal separately,

TABLE IV

ESTIMATED VITAMIN C INTAKE OF BASE POST OFFICE TROOPS PER MEAL

Range of intake— milligrams	Percentage of individuals			
	February 10th		February 11th	February 12th
	Dinner	Supper	Dinner	Dinner
0 to 5	36	26	32	30
5 " 10	64	1	24	27
10 " 15	..	20	38	37
15 " 20	..	41	6	6
20 " 25	..	11	..	..
Over 25	..	1	..	..

further estimates may be made of the range of total individual intake from dinner and supper of each day, on the assumptions (*a*) that the choice of vegetables at supper by each man was statistically independent of his selection at dinner, and (*b*) that the scale of intake at supper on February 11th (beef stew and boiled potatoes) was equivalent to that at dinner on February 10th (boiled potatoes and carrots), the latter assumption being almost certainly over-optimistic. Thus for example in these circumstances, of the 26 per cent of individuals receiving an estimated 0 to 5 mg. from their consumption of vegetables at supper on February 10th, 26 × 36/100 or 9 per cent may be computed likewise to have had an estimated intake of 0 to 5 mg. at the preceding meal, and hence a possible combined intake of 0 to 10 mg. On the other hand 26 × 64/100 or 17 per cent had received an estimated 5 to 10 mg. at dinner and consequently had a possible combined intake of 5 to 15 mg. It will be noted that there is now some overlapping in the successive derived categories of possible intake, viz. 0 to 10, 5 to 15, 10 to 20 mg. etc.; but even if it be favourably assumed that none of the individuals in the class 5 to 15 mg. actually consumed less than 10 mg., that none of those in the class 15 to 25 mg. actually consumed less than 20 mg., etc., the estimated scale of daily intake would still be as indicated in Table V.

TABLE V

ESTIMATED DAILY VITAMIN C INTAKE OF BASE POST OFFICE TROOPS FROM VEGETABLES EATEN

Daily intake, milligrams	Percentage of individuals			
	February 10th	February 11th	February 12th	Average
Less than 10	9	12	8	10
" " 20	34	70	30	45
" " 30	92	100	72	88
" " 40	99	..	98	99

These estimates may if anything still be somewhat optimistic by virtue of the fact that they assume, as explained above, a statistically independent choice of vegetables at dinner and supper of each day. In actuality it is likely that a certain proportion of the men had a definite distaste for any vegetable other than potatoes, and hence took potatoes only at both meals in somewhat greater numbers than calculated from chance probability. This would tend to increase the proportion of individuals in the lowest categories of vitamin intake. Moreover, as the remaining vegetables served during the week, viz. boiled

beets and baked beans, the former after cooking were of the same order as cabbage and turnips, and the latter were entirely negligible as sources of ascorbic acid, the indications were that this condition was chronic during the winter period.

Vitamin C Intake of District Depot Troops

Observations were made in the District Depot kitchen and mess hall on three successive days in February, when vegetables were served in the average amounts indicated: February 23rd, dinner: boiled potatoes (130 g.) and cabbage (80 g.); supper: potatoes (99 g.) and coleslaw containing cabbage, carrot, onion and vinegar (90 g.); February 24th, dinner: boiled potatoes (133 g.) and carrots (62 g.); supper: potatoes, some boiled, some fried (94 g.) and green peas, boiled (34 g.), served with roast beef sandwich; February 25th, dinner: boiled potatoes and turnips; supper: potatoes, some boiled, some fried (111 g.) and cold tomatoes (117 g.)

The deduced statistics of consumption of these are listed in Table VI. With

TABLE VI

PERCENTAGE OF DISTRICT DEPOT TROOPS IN VARIOUS CATEGORIES OF VEGETABLE CONSUMPTION

Consumption category	February 23rd		February 24th		February 25th	
	Dinner	Supper	Dinner	Supper	Dinner	Supper
Took no vegetable	½	2½	½	½	1	½
Took potatoes only, ate entire serving	13	11	12½	½	15½	13
Took potatoes only, left some uneaten	2	4	2½	½	2	3½
Took second vegetable only, ate entire serving	1½	1½	½	6	½	½
Took second vegetable only, left some uneaten	½	½	..	½	½	..
Took both vegetables, ate entire serving of both	50	31	34	58½	30	45½
Took both vegetables, ate all of second, left some potatoes	11	20	13	20	9	16
Took both vegetables, ate all potatoes, left some of second vegetable	10	13	11	7	17	6
Took both vegetables, left some of both	12	16	26	6	24	15
Took two servings of second vegetable	..	½	..	½	½	½
Took two servings of potatoes	..	..	..	½	½	..
Took two servings of both vegetables	..	..	..	½	..	..
Took one serving of potatoes, two of second vegetable	..	..	..	..	..	½
Number of men enumerated	685	496	724	558	750	536

one exception (supper on February 24th, when the meat courses consisted of a roast beef sandwich), the indicated habits of vegetable consumption were similar to those prevailing in the Base P.O. unit, 15 to 20 per cent of the men taking potatoes only (as compared however to a maximum of 30 per cent in the B.P.O.) and not more than 50 per cent eating an entire serving of both vegetables at any given meal. The average recorded weights of uneaten residues are listed in Table VII. From these, it would appear that tomatoes were the most palatable and turnips the least palatable of the seven vegetables examined.

Using the same method of computation as before, the scale of individual vitamin C intake listed in Table VIII was arrived at for each meal. The contrast in intake from cooked and uncooked cabbage (coleslaw) is notable. Both carrots and peas are relatively poor sources of vitamin C. Actually the peas as served had a content 2½ times that of the carrots, but this was offset by the fact that the average portion of the former weighed only 34 g. Whilst

TABLE VII

VEGETABLE RESIDUES LEFT UNEATEN BY DISTRICT DEPOT TROOPS

Vegetable	Percentage of men		Average weight of serving, grams	Average weight of residue, grams	Average residue as per cent by weight of average serving
	Taking serving	Leaving residue			
Potatoes	95	34	116	49	42
Cabbage	84	22	80	32	40
Carrots	84	37	62	25	40
Coleslaw	82	29	90	39	43
Peas	98	14	34	12	35
Tomatoes	84	21	117	32	27
Turnips	81	41	62	35	56

TABLE VIII

ESTIMATED VITAMIN C INTAKE OF DISTRICT DEPOT TROOPS PER MEAL

Range of intake, milligrams	Percentage of individuals					
	February 23rd		February 24th		February 25th	
	Dinner	Supper	Dinner	Supper	Dinner	Supper
0 to 5	26	20	69	99¾	85	17
5 " 10	71	3	31	¼	15	3
10 " 15	3	3	..	..	..	7
15 " 20	..	6	..	..	..	26
20 " 25	..	10	..	..	..	34
25 " 30	..	12	..	..	..	10
30 " 35	..	17	..	..	..	2
35 " 40	..	15	..	..	..	1
Over 40	..	14	..	..	..	..

notably superior to that from any of the cooked vegetables, the intake from tomatoes was not equal to that from coleslaw.

The scale of individual daily intake was deduced to be as shown in Table IX. The superiority of coleslaw as a source of vitamin C is clearly reflected

TABLE IX

ESTIMATED DAILY VITAMIN C INTAKE OF DISTRICT DEPOT TROOPS FROM VEGETABLES EATEN

Daily intake, milligrams	Percentage of individuals			
	February 23rd	February 24th	February 25th	Average
Less than 10	5	69	14	29
" " 20	24	100	26	50
" " 30	34		82	72
" " 40	57	..	99	85
Over 40	43	..	1	15

in the results for February 23rd, on which day it seems likely that about half the men had an intake of at least 40 mg. Even on this occasion, however, it is estimated that one-quarter of the men received less than 20 mg., and in view of the much less favourable results deduced for February 24th and 25th, together with the fact that the only other vegetable appearing on the diet sheet at this time, namely boiled beets, is inferior to tomatoes in ascorbic acid content, it must be concluded that on the average at least 70 per cent of the men were in receipt of less than 30 mg. daily intake from vegetable sources.

Effect of Conservation of Vitamin C on Estimated Intake

It is possible by means of improved cooking methods to conserve more of the vitamin C content of the vegetables served. This would have a marked effect on the level of daily intake of the men. It could not, however, be expected to eliminate completely the deficiencies indicated in the preceding

section as will be appreciated when it is recollected that at each meal surveyed, 15 to 30 per cent of the men ate potatoes only or no vegetable at all.

As a matter of interest, the estimated range of daily intake shown in Table X was computed on the basis of the observed amounts of vegetables actually

TABLE X

ESTIMATED INTAKE OF TROOPS, ASSUMING 50 PER CENT RETENTION OF ORIGINAL VITAMIN C CONTENT OF VEGETABLES

Daily intake, milligrams	Percentage of individuals			
	Base Post Office			Base Depot
	February 11th	February 12th	Dinner, Feb. 11th Supper, Feb. 12th	February 23rd
Less than 10	1	2	1	1
" " 20	36	16	12	5
" " 30	59	55	41	10
" " 40	94	84	67	26

consumed on the days indicated, but assuming that 50 per cent of the original vitamin content was retained in the material served. Had the cabbage and potatoes served at the Base Post Office on February 11th occurred in conjunction with an evening meal including cold tomatoes and potatoes, as on February 12th, the computed range of intake would have been as shown in column four of the table, and 40 per cent of the men still would have been in receipt of less than 30 mg.

At the Base Depot on February 23rd, 26 per cent of the men would have received less than 40 mg. This, however, represents the range of intake that might be expected when the two richest sources of vitamin C in the available dietary were served on the same day, i.e. boiled cabbage at dinner and coleslaw at supper. The results for other vegetables would approximate more closely those computed for the Base P.O. unit on February 11th and 12th.

In view of the observed dietary habits and in the absence of sources other than the vegetables served, an appreciable number of individuals could be expected to have a daily intake of less than 40 milligrams of vitamin C.

SUMMARY

Analytical and statistical data obtained from surveys conducted during the winter of 1941-42 have been used to estimate the individual daily intake of vitamin C from vegetable sources included in the regular issue of army garrison rations, by troops of two units in Ottawa. Current methods of cooking left only a small fraction of the original vitamin C concentration in the food as served.

Of the troops served, 15-30 per cent refused any vegetable other than potatoes and about 1 per cent took no vegetable. In some instances, as high as 50 per cent of the men failed to eat the entire serving they received; the uneaten residues averaged from 15 per cent by weight of the average original serving for tomatoes to 56 per cent for turnips.

From the foregoing facts it was estimated that about 88 per cent of the men in one unit and 70 per cent of those in the other had a daily vitamin C intake of less than 30 mgs. from vegetable sources. Increased retention of vitamin C in cooking will not overcome deficiencies arising from consumption habits.

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The Adaptation of Mycobacterium Paratuberculosis to Artificial Culture Media Prepared Without the Addition of the "Essential Substance"

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MYCOBACTERIUM PARATUBERCULOSIS (Johne's bacillus), the causative agent of chronic paratuberculous enteritis of cattle and sheep, closely resembles morphologically and culturally the human and bovine tubercle bacillus. It is distinguished from them by the absence of pathogenicity towards small laboratory animals and by the fact that its isolation from the natural host is possible only on culture media to which has been added a growth factor. This so-called "essential substance" is supplied by the heat-killed cells of certain other members of the acidfast group or by glycerine extracts of them. *M. phlei* has been found most suitable for this purpose.

Although Twort and Ingram (1) had succeeded in adapting one of their strains to ordinary glycerine bouillon, their finding received little attention and until recently it was considered necessary to add the growth factor to the various solid or liquid media in order to successfully propagate *M. paratuberculosis.*

The method formerly used for the preparation of johnin, the diagnostic agent of paratuberculous enteritis, was to cultivate the causative organism on a liquid medium to which had been added the essential growth factor and to process the resulting product in a manner similar to that used in preparing tuberculin. This had the disadvantage of introducing a distinctly heterologous bacillary substance. Frequent non-specific reactions observed led to an attempt to adapt *M. paratuberculosis* to various synthetic liquid media prepared without the addition of the growth factor.

In 1933 Dunkin (2) reported delayed and meagre growth in a first subculture on Henley's medium. The possibility cannot be excluded, however, that growth at this early stage of adaptation was due to the small amount of the growth factor transferred with the inoculum from the parent culture. In 1935, Watson (3) reported the adaptation of five old laboratory strains of *M. paratuberculosis* to Long's synthetic medium adjusted to pH 5.6-5.8, as well as to potato Long's medium. Since then, McCarter and Hastings (4) obtained growth on Dorset's synthetic medium which was carried on for ten generations but decreased in luxuriance and changed in character. More recently, Hagan (5) has achieved acclimatization to Dorset's, Henley's and Moskey's medium and

Presented at the twelfth annual Christmas meeting of the Laboratory Section, Canadian Public Health Association, held in the Royal York Hotel, Toronto, on December 15 and 16, 1943.

Glover (6) has prepared johnin from cultures grown on ordinary Henley's synthetic medium.

The five cultures reported on by Watson required varying periods of time for their adaptation. The results of these trials are summarized in Table I. The fact that all were old laboratory strains suggested that a prolonged cultivation outside the animal body might be a prerequisite for successful acclimatization.

More recent work carried out in this Institute with seven freshly isolated strains indicated that this is unnecessary. These strains were isolated from different sources in Canada and attempts to cultivate them without the essential growth factor were made as soon as substantial development was obtained on special egg or agar medium containing *M. phlei* extract. The results of these trials are summarized in Table II.

TABLE I

ADAPTATION OF FIVE OLD LABORATORY STRAINS OF JOHNE'S BACILLUS TO POTATO LONG'S— AND LONG'S SYNTHETIC MEDIUM

Strain No.	Origin and date Received	Adaptation to			
		Pot. Long's synth. med.		Long's synth. med.	
		Date	Time (months)	Date	Time (months)
I (165)	Vallée April 1928	January 1930	21	June 1930	26
II (166)	Dunkin September 1929	June 1930	9	February 1933	41
III (167)	Hastings October 1928	December 1929	14	March 1930	17
IV (168)	Vallée June 1929	January 1930	7	October 1933	52
V (218)	Hastings May 1931	September 1931	4	July 1933	26

When comparing the time-periods required for the adaptation of the five old laboratory strains (Table I) with those of the seven freshly isolated cultures (Table II), no marked difference is noted. In both series some cultures required longer than others to fully establish themselves on plain Long's synthetic liquid, while that necessary for their education on potato medium was more alike and in general considerably shorter. The latter medium has proved more suitable for this purpose and has given satisfactory results in the maintenance of adapted stock cultures of *M. paratuberculosis*.

The question arises whether cultivating the acclimatized strains on medium which does not contain the essential growth factor may bring about changes in the morphological and biological properties of the organism and establish a stable variant. One of the group of the five old laboratory strains has shown changes suggestive of this possibility (7). It will suffice to say that the gross

cultural appearance of this strain has become smooth and slightly folded, in contrast to the granular, knobby type of growth shown by other strains. It also produces an alkaline reaction curve in Long's synthetic liquid and resembles in this respect the S-variant of avian tubercle bacillus (8). The yield of bacillary growth and johnin P.P.D. obtained from this strain is much less than that harvested from the characteristic granular, knobby cultures. Also the potency of the johnin P.P.D. is lower when titrated on sensitized guinea pigs.

The adapted *M. paratuberculosis* cultures do not grow as luxuriantly on Long's synthetic medium as do bovine and human tubercle bacilli. The excellent results obtained by Dorset in the cultivation of a human strain (9) led to the consideration that the growth requirements of *M. paratuberculosis* might be

TABLE II

ADAPTATION OF SEVEN FRESHLY ISOLATED STRAINS OF JOHNE'S BACILLUS TO POTATO LONG'S— AND LONG'S SYNTHETIC MEDIUM

Identification of Strain	Origin and date Isolated	Adaptation to			
		Pot. Long's synth. med.		Long's synth. med.	
		Date	Time (months)	Date	Time (months)
C. 300	A.D.R.I. May 1934	May 1935	12	January 1936	20
C. 286	A.D.R.I. July 1935	May 1936	10	December 1936	17
C. 287	A.D.R.I. September 1936	April 1938	19	December 1938	27
Waldie Estate	A.D.R.I. December 1937	October 1938	10	November 1940	35
Simpson	A.D.R.I. December 1938	January 1940	13	Adaptation not attempted.	
O'Brien	A.D.R.I. December 1939	January 1941	13		
Emerson	A.D.R.I. May 1940	January 1941	8		

better supplied by a combination of the nutriments offered in Dorset's medium. To determine this point six adapted strains were carried in series for approximately 2½ years. As the effect of sugar on the development of *M. paratuberculosis* had been variously described as inhibitory or stimulating, the 1 per cent dextrose called for in the original Dorset's formula was omitted in one series while it was retained in the other. Each of the two media was tried at four different pH adjustments ranging from 5.5 to 7.6. The cultivation of the six strains of *M. paratuberculosis* was thus carried out on a total of eight series.

Briefly summarized, the results of these cultural trials indicated that excepting one strain the luxuriance of *M. paratuberculosis* on Dorset's medium or any

modification of it used was below that obtained on Long's synthetic liquid. One strain developed with greater speed and luxuriance on Dorset's medium which contained sugar and which had been adjusted to pH 7.4-7.6. In the remaining five strains the most suitable adjustment was around the neutral point. The addition of sugar exerted in some a stimulating and in others an inhibitory influence. The trials therefore would appear to indicate that the use of Dorset's medium offers no advantage over Long's synthetic liquid for the propagation of *M. paratuberculosis.*

Summary

(1) The adaptation of seven freshly isolated strains of *M. paratuberculosis* to Long's synthetic medium prepared without the addition of the "essential substance" has required an average time period approximately equal to that needed for a similar adaptation of five old laboratory strains of the organism.

(2) This fact suggests that *M. paratuberculosis* may be adapted in a comparatively short time after its isolation from the natural host to suitable plain artificial media.

(3) Although some variability may occur in occasional strains due to the prolonged cultivation on such media, most strains retain their original gross cultural characteristics and are suitable for the production of a potent diagnostic agent.

(4) Trials to increase the luxuriance of adapted strains of *M. paratuberculosis* by cultivation on Dorset's synthetic medium at various pH levels were unsuccessful.

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Bacteriostatic Activity of Citrinin in Vitro[1]

M. I. TIMONIN[2] AND J. W. ROUATT[3]

IT has been reported from this laboratory (15, 16) that *Aspergillus sp.* of the *Candidus* group was able to produce a bacteriostatic substance, citrinin. Raistrick and Smith (11), Oxford (10) and Tauber *et al* (14) reported that citrinin obtained from the metabolism solution of *Penicillium citrinum* Thom possesses bacteriostatic properties and is able to inhibit growth of *Staphylococcus aureus* in dilutions of 1:50,000. The present investigation was planned with the object of obtaining information concerning the bacteriostatic activity of citrinin obtained from the metabolism solutions of *Aspergillus sp.*

Production of Citrinin

The composition of the medium and yield of citrinin on surface cultures has been reported elsewhere (16). However, using the Kluyver and Perquin's (5) shaking culture method, which has been successfully applied by Weindling (18) for production of mold toxin of *Gliocladium* and *Trichoderma,* this organism failed to produce substantial amounts of citrinin.

The influence of different sugars and length of time of incubation on the bacteriostatic potency of metabolic solutions and the yield of crude citrinin is shown in Graph 1. Gradual increase in potency was noted up to 20 days' incubation. Further incubation did not increase the potency of the solution, whereas the yield of citrinin continued to rise until the 28th day, after which a decrease in yield was noted in glucose and honey media.

Method of Assay

The assay of the metabolism solutions and the crystalline preparations of citrinin was carried out by the dilution method. Four ml. of assay medium were pipetted into a series of test tubes to which different amounts of a standard solution of citrinin were added. Due to the sparing solubility of citrinin in water it was dissolved in the following solvents:

(1) Saline sodium citrate ($NaC_6H_5O_7.2H_2O$—1.05 per cent and NaCl—0.8 per cent).

(2) Phosphate buffer—(50 ml. M-5 KH_2PO_4; 35 ml. M/5 NaOH mixed and brought up to 200 ml. with distilled H_2O).

(3) Alkaline water (pH 8 to 10).

These solutions were brought to the boiling point to assure sterility and at the same time to hasten the solubility of the citrinin. In these solvents it was possible to obtain concentrations up to 1:300. For routine analyses, however, 1.4,000 or 1:8,000 dilutions were used as standard concentrations.

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Peptone water (1 per cent peptone and 0.5 per cent NaCl) and nutrient broth, plain or with addition of 1 per cent glucose, were used as assay media. In preparing the inoculum, 4 ml. of assay medium was inoculated with a 24-hour nutrient agar culture and incubated 24 hours at 37°C. After two successive passages (24 hours each) the cultures were thoroughly mixed and by means of a standard loop (0.004 ml.) the serial dilutions were inoculated. Inoculated tubes were incubated for 18 and 42 hours and examined for visible turbidity. The limiting dilutions which showed no growth were recorded as a point of maximum bacteriostatic activity.

TABLE I

BACTERIOSTATIC ACTIVITY OF CITRININ

Organism	Limiting dilution for complete inhibition of growth	
	18 hours	*48 hours*
B. mycoides	128,000	128,000
B. subtilis 245	200,000	200,000
" " 246	33,000	33,000
" " W*	60,000	
E. coli	2,000	2,000
E. typhimurium	4,000	4,000
E. typhosa	2,000	2,000
Ps. aeruginosa	8,000	4,000
Staph. albus 457	50,000	40,000
" *citreus* 17	80,000	50,000
" *aureus* 292	65,000	50,000
" " 458	160,000	160,000
" " 459	80,000	66,000
" " 7c	125,000	80,000
" " 11c	100,000	100,000
" " 117	50,000	16,000
" " 605	25,000	16,000
" " 610	12,000	10,000
" " 620	12,000	10,000
" " W*	40,000	
Str. haemolyticus Group A Type 1 (SF 130)**	18,000	16,000
Str. haemolyticus Group A Type 2 (S.F. 22)**	12,000	12,000
Str. haemolyticus Group A Type 3 (KL 56)**	18,000	12,000

*Determined by S. A. Waksman.
**Determined by E. T. Bynoe.

BACTERIOSTATIC PROPERTIES OF CITRININ

All data presented in this report are the results of experiments with crystalline citrinin obtained by the hot alcohol method or as otherwise stated. During the course of investigations it was found that different organisms as well as different strains of the same species showed different degrees of susceptibility to citrinin. As shown in Table I, Gram-negative organisms tested were resistant to citrinin. The most susceptible strain among the staphylococci tested proved to be *Staph. aureus* 458, and this strain was used as test organism in all experiments reported in this paper, except as otherwise stated.

The effect of the assay media on the bacteriostatic properties of antibiotic substances has been considered by several workers. However, their effect on citrinin, as far as the authors are aware, was not investigated. The results summarized in Table II indicate that the organism is less resistant to citrinin in peptone water than in nutrient broth. The addition of glucose (1 per cent) to both media enhanced somewhat the potency of citrinin.

It has been pointed out that citrinin is only sparingly soluble (1:25,000) in hot or cold water. However, it is quite soluble in saline sodium citrate solution, phosphate buffer (pH 7.0) and alkaline water, and moderately soluble in nutrient broth. The effect of the above-mentioned solvents on the bacteriostatic power

TABLE II

EFFECT OF ASSAY MEDIUM ON ACTIVITY OF CITRININ

Media	Limiting dilution for complete inhibition of growth of *Staph. aureus* 458	
	18 hours	*42 hours*
Peptone water	200,000	130,000
Peptone water + glucose 1%	250,000	135,000
Nutrient broth	125,000	76,000
N. B. + glucose (1%)	165,000	100,000

Citrinin used in all cases except otherwise stated was of crystalline form of hot alcohol preparation and dissolved in sodium citrate solution.

TABLE III

EFFECT OF DIFFERENT SOLVENTS ON ACTIVITY OF CITRININ

Solvents	Limiting dilution for complete inhibition of growth of *Staph. aureus* 458			
	Nutrient broth		N. B. + glucose (1%)	
	18 hours	42 hours	18 hours	42 hours
Nutrient broth	80,000	80,000	160,000	160,000
Sod. citrate solution	125,000	76,000	165,000	100,000
Phos. buffer solution	113,000	63,000	129,000	107,000
Alkaline water	108,000	52,000	118,000	82,000

of citrinin is summarized in Table III. The data indicate that sodium citrate is a solvent which does not interfere (or interferes to a lesser degree) with the bacteriostatic potency of citrinin.

It has been reported elsewhere (16) that citrinin can be purified by three methods, (1) the hot alcohol method of Hetherington and Raistrick, (2) the dioxane method of Tauber, and (3) a modification of the hot alcohol method developed in this laboratory (alcohol method). Data summarized in Table IV indicate the bacteriostatic activity of preparations dissolved in different solvents. It seems that the "hot alcohol" preparation is somewhat more potent than the others when assayed in nutrient broth. In the majority of cases the addition of

glucose to the assay medium enhanced the potency of all preparations as compared with plain broth.

The hydrogen ion concentration of the standard 25 mgm. per cent solutions of citrinin of different preparations as shown in Table V did not vary to any appreciable extent with different solvents except in the case of alkaline water. In general the data indicate the acid nature of citrinin; however, the hydrogen ion concentration of different standard solutions except in the case of alkaline water is in the range of the required pH of medium for the maximum growth of staphylococci.

The bactericidal effect of citrinin on growing cultures of *Staph. aureus*

TABLE IV

BACTERIOSTATIC ACTIVITY OF CITRININ OF DIFFERENT PREPARATIONS AS INFLUENCED BY DIFFERENT SOLVENTS

Citrinin preparations	Limiting dilution for complete inhibition of *Staph. aureus* 458			
	Nutrient broth		N. B. + glucose (1%)	
	18 hours	42 hours	18 hours	42 hours
Dissolved in sodium citrate				
Hot alcohol	125,000	76,000	165,000	100,000
Dioxane	80,000	50,000	80,000	33,000
Alcohol	80,000	33,000	165,000	125,000
Unpurified	125,000	50,000	125,000	125,000
Residue	20,000	20,000	20,000	20,000
Dissolved in phosphate buffer				
Hot alcohol	113,000	63,000	129,000	107,000
Dioxane	50,000	33,000	165,000	65,000
Alcohol	50,000	33,000	165,000	65,000
Unpurified	50,000	33,000	125,000	65,000
Residue	20,000	20,000	20,000	20,000
Dissolved in alkaline water				
Hot alcohol	108,000	52,000	118,000	82,000
Dioxane	65,000	33,000	165,000	125,000
Alcohol	65,000	33,000	100,000	65,000
Unpurified	65,000	33,000	165,000	100,000
Residue	33,000	25,000	33,000	25,000

was also studied in a series of quantitative determinations by the plate method. of organisms surviving following treatment of 16-hour cultures growing in plain nutrient broth. The 16-hour culture was subdivided into 50-ml. portions and counts were made to note the effect of citrinin and sugars after a further incubation period of 6, 24, 30 and 48 hours. The results are summarized in Graph 2.

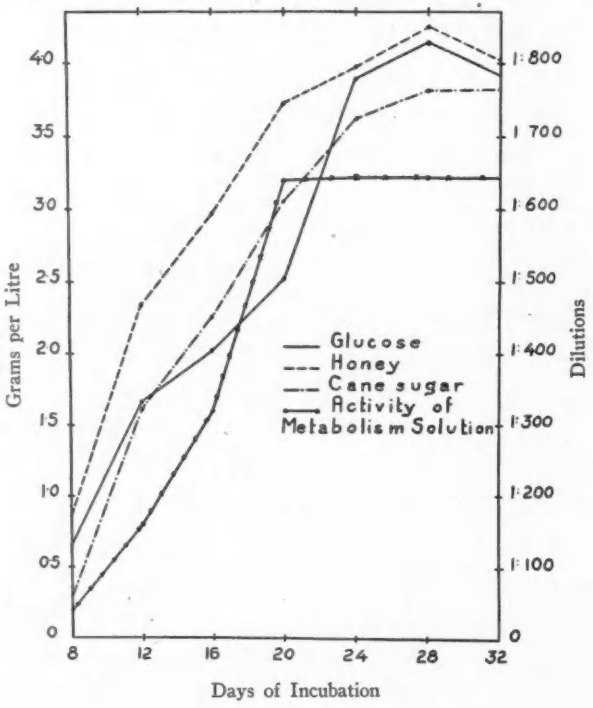
The addition of 100 γ /ml. of citrinin resulted in reduction of numbers of surviving cells to 66.6, 39.4, 26.0 and 5.7 per cent of those present at the start, after incubation of 6, 24, 30 and 48 hours respectively. Addition of 200 γ /ml. under similar conditions resulted in the following reductions: 48.7, 26.4, 17.9

and 4.2 respectively. One per cent of glucose considerably enhanced the bactericidal effect of citrinin. However, glucose alone reduced the numbers of cells surviving after 48 hours' incubation to 2.2 per cent of the original number, an effect doubtless due to the acidity produced with the longer incubation.

Addition of 1 per cent sucrose had no influence on the effect of citrinin at a concentration of 200 γ /ml. on the numbers of surviving organisms. Control-sucrose cultures showed the same trend as those in plain broth with considerably higher numbers.

GRAPH 1

Effect of Different Sugars and Length of Incubation at 28°C. on the Bacteriostatic Potency of Metabolism Solutions and Yield of Citrinin.



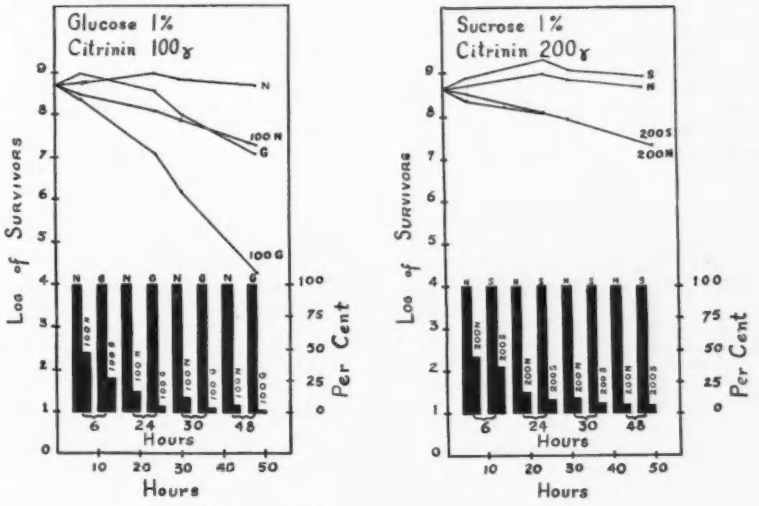
The hydrogen ion concentration of cultures containing glucose after 48 hours' incubation was considerably higher (pH 3.2 - 3.8) than that of nutrient broth (pH 5.8).

It has been previously reported (15) that autoclaving of serial dilutions for 30 minutes at 15-lb. pressure did not destroy the bacteriostatic activity of citrinin. This experiment was repeated and data summarized in Table VI confirm previous findings.

To study the influence of time of incubation at 37°C. prior to inoculation of test organism, on the bacteriostatic activity of citrinin several sets of serial dilutions were prepared and treated as follows: one set inoculated immediately after preparation, a second incubated for 24 hours and a third for 48 hours prior to inoculation. Records of complete inhibition of growth in the limiting dilutions were made after 24, 48 and 72 hours' incubation. The results summarized in Table VII indicate that the assay medium has a considerable

GRAPH 2

EFFECT OF CITRININ AND SUGARS ON GROWING CULTURES OF *Staph. aureus* 458



N = Nutrient Broth
G = Nutrient Broth + 1% Glucose
100N = Nutrient Broth + 100 /ml. Citrinin
100G = Nutrient Broth + 1% Glucose + 100 /ml. Citrinin
200N = Nutrient Broth + 200 /ml. Citrinin
S = Nutrient Broth + 1% Sucrose
200S = Nutrient Broth + 1% Sucrose + 200 /ml. Citrinin

Black columns illustrate the comparison of numbers of colonies obtained from control flasks and corresponding flasks containing citrinin. The numbers of colonies obtained from control flasks are expressed as 100 and from corresponding flasks containing citrinin expressed on the percentage basis of the controls.

influence on the bacteriostatic activity of citrinin. Thus in plain peptone water 48 hours' pre-incubation reduced the titre from 250,000 to 100,000. A series of dilutions prepared with nutrient broth, on the other hand, showed reduction in potency only after 96 hours' incubation. Autoclaving of one per cent glucose with media acted as a protective agent.

The addition of 5 per cent fresh horse serum as shown in Table VIII decreased the potency of citrinin in peptone water and nutrient broth, plain or with addition of glucose. However, it seems from the data presented in

Table IX that 20 γ/ml. of p-aminobenzoic acid (PAB) had no influence on the potency of citrinin.

Toxicity of Citrinin

The toxicity of citrinin *in vivo* was tested by Dr. R. L. Noble of McGill University. The solutions of citrinin were prepared as follows. Crystals

TABLE V

Hydrogen Ion Concentration of Citrinin Solutions

Citrinin preparations	Na citrate solution		Phos. buff. solution		Alkaline water solution	
	Cont.	+ Cit.	Cont.	+ Cit.	Cont.	+ Cit.
Crystalline	7.50	6.90	6.90	6.85	10.80	10.20
Dioxane	do	7.00	do	6.90	9.90	7.25
Alcohol	do	6.90	do	7.00	10.40	9.80
Residue	do	7.00	do	6.90	10.00	8.10
Unpurified	do	6.90	do	6.90	10.70	10.40

TABLE VI

Effect of Autoclaving (20 min., 15 D/lbs.) on Activity of Citrinin Against Staphylococci

Test organism	Treatment	Dilution of citrinin in thousands								
		1	2	4	8	16	32	64	128	256
Staph. aureus 292	Autoclaved	−	−	−	−	−	−	−	+	+
	Not autoclaved	−	−	−	−	−	−	−	+	+
Staph. albus 457	Autoclaved	−	−	−	−	−	−	−	+	+
	Not autoclaved	−	−	−	−	−	−	−	−	+

+ = growth; − = no growth.

TABLE VII

Effect of Pre-incubation Prior to Sowing Test Organism on Activity of Citrinin

Read after Incubation (hrs.)	Media	Limiting dilution for complete inhibition of growth		
		Incub. prior to inoc. test org.		
		0 hour	24 hours	48 hours
24	Peptone water	250,000	125,000	100,000
	Peptone glucose water	250,000	250,000	250,000
	Nutrient broth	100,000	100,000	100,000
	N. B. glucose	250,000	125,000	250,000
48	Peptone water	125,000	100,000	100,000
	Peptone glucose water	250,000	125,000	250,000
	Nutrient broth	100,000	100,000	100,000
	N. B. glucose	250,000	125,000	250,000
72	Peptone water	125,000	80,000	100,000
	Peptone glucose water	250,000	125,000	250,000
	Nutrient broth	100,000	80,000	80,000
	N. B. glucose	250,000	100,000	125,000

TABLE VIII

EFFECT OF FRESH HORSE SERUM (5 PER CENT) AND ASSAY MEDIA ON ACTIVITY OF CITRININ

Media	Dilution of citrinin in thousands										
	12	20	25	33	50	66	100	125	165	200	250
Inoculated immediately											
Peptone	−	−	−	−	−	−	−	−	−	−	−
Peptone + serum	−	∓	+	+	+	+	+	+	+	+	+
Peptone + glucose	−	−	−	−	−	−	−	−	−	−	−
Peptone + glucose + serum	−	−	−	+	+	+	+	+	+	+	+
Nutrient broth	−	−	−	−	−	−	−	−	+	+	+
Nutrient broth + serum	−	−	+	+	+	+	+	+	+	+	+
Nutrient broth + glucose	−	−	−	−	−	−	−	−	−	−	−
N. B. + glucose + serum	−	−	−	+	+	+	+	+	+	+	+
Inoculated after 18 hours incubation at 37°C.											
Peptone	−	−	−	−	−	−	−	−	+	+	+
Peptone + serum	−	+	+	+	+	+	+	+	+	+	+
Peptone + glucose	−	−	−	−	−	−	−	−	−	+	+
Peptone + glucose + serum	−	±	+	+	+	+	+	+	+	+	+
Nutrient broth	−	−	−	−	−	−	−	+	+	+	+
Nutrient broth + serum	−	+	+	+	+	+	+	+	+	+	+
Nutrient broth + glucose	−	−	−	−	−	−	−	−	−	+	+
Nutrient broth + glucose + serum	−	−	±	+	+	+	+	+	+	+	+

TABLE IX

EFFECT OF P.A.B. (20γ/ML.) AND SOLVENTS ON ACTIVITY OF CITRININ

Media	Dilution of citrinin in thousands								
	10	12	16	25	50	80	100	125	250
Na citrate									
Peptone	−	−	−	−	−	−	−	−	−
Peptone + PAB	−	−	−	−	−	−	−	−	−
Peptone + glucose	−	−	−	−	−	−	−	−	+
Peptone + glucose + PAB	−	−	−	−	−	−	−	−	+
Nutrient broth	−	−	−	−	−	−	−	−	+
Nutrient broth + PAB	−	−	−	−	−	−	−	+	+
Nutrient broth + glucose	−	−	−	−	−	−	−	−	+
N. B. + glucose + PAB	−	−	−	−	−	−	−	+	+
Phosphate buffer									
Peptone	−	−	−	−	−	−	−	±	±
Peptone + PAB	−	−	−	−	−	−	−	−	−
Peptone + glucose	−	−	−	−	−	−	−	±	+
Peptone + glucose + PAB	−	−	−	−	−	−	±	+	+
Nutrient broth	−	−	−	−	−	−	+	+	+
Nutrient broth + PAB	−	−	−	−	−	−	−	±	±
Nutrient broth + glucose	−	−	−	−	−	−	−	±	+
N. B. + glucose + PAB	−	−	−	−	−	−	−	−	+
Alkaline water									
Peptone	−	−	−	−	−	−	−	−	+
Peptone + PAB	−	−	−	−	−	−	−	−	±
Peptone + glucose	−	−	−	−	−	−	−	±	+
Peptone + glucose + PAB	−	−	−	−	−	−	−	−	+
Nutrient broth	−	−	−	−	−	−	−	−	+
Nutrient broth + PAB	−	−	−	−	−	−	−	±	+
Nutrient broth + glucose	−	−	−	−	−	−	−	+	+
N. B. + glucose + PAB	−	−	−	−	−	−	−	+	+

were dissolved in NaOH solution (pH 8-9.5). The solutions were then brought back to neutral reaction as rapidly as possible by the addition of HCl. Adult mice 20 gm. in weight were used and the volume of solution injected was 0.5 ml. The results obtained are summarized as follows:

No. of mice	Dose in mgs. intraper.	Mortality %	Remarks
5	2.5	100	Death in 5- 6 hours
5	2.0	100	Death in 6-18 hours
5	1.0	0	Dose repeated 24 hours later with mortality 40 per cent
5	0.5	0	
5	2.0 subcut.	80	Death in 4-24 hours
5 rats	50 mgs. per kg. i.p.	0	

Furthermore, Dr. Noble reported that "gross inspection of the dead mice revealed no obvious changes. The experiment with the mice showed a sharp level dosage which caused mortality. Animals which survived with the smaller doses appeared to be generally ill."

During the course of the investigation on the toxicity of citrinin in this laboratory it was found that 90 mgs. of citrinin dissolved in sodium citrate solution and administered during 24 hours to a rabbit (3.485 kg.) in two doses *per os* by means of catheter resulted in no ill effect to the animal. At the same time a second rabbit received subcutaneously 30 mgs. of citrinin, dissolved in 10 ml. solution, daily for five days. This treatment also resulted in no ill effects.

Discussion

During the course of the investigation of bacteriostatic activity of citrinin *in vitro* two points of interest for discussion were noted: the enhanced potency of citrinin on addition of glucose to the assay medium and the inability of p-aminobenzoic acid to inactivate the antibacterial potency of citrinin.

Apart from the relation of glucose to the antibacterial action of notatin (12, 17), the addition of glucose has been found to enhance the potency of other antibiotic substances. Thus Oxford (10) reported that the addition of glucose to the assay medium enhanced the potency of penicillic acid. In explanation of this phenomenon he stated that when glucose is sterilized with the assay medium, such as heart broth containing peptone, it combines during the sterilization with certain substances of the medium which without the addition of glucose remain free and would react with penicillic acid, resulting in deterioration of the latter. Several workers have shown that assay media containing peptone are inhibitory to the bacteriostatic activity of sulpha drugs (10, 18). Thus it seems that a purely chemical reaction takes place between peptone and glucose during sterilization which lessens the inhibitory function of peptone. Foster and Wilker (2), on the other hand, working with bacteriostatic properties of penicillin, concluded that glucose does not react with the assay medium but rather with penicillin, causing its partial inactivation. They stated further that this reaction occurs only over small concentrations of penicillin, whereas higher

concentrations were unaffected by the presence of glucose, which is in accordance with the findings of this laboratory (8). The evidence in this report indicates a similarity to Oxford's findings that glucose when sterilized with the assay medium protects the effectiveness of citrinin.

The theory of resistance of bacteria to the sulpha drugs proposed by Fildes (1) and Woods (20) was based on the assumption that sulpha drugs inhibit bacterial growth by interfering with the utilization of p-aminobenzoic acid (PAB) by virtue of their similarity in structure to this compound. Furthermore, Landy *et al.* (6, 7,) and Spink and Vivino (13, 18) reported that different strains of *Staph. aureus* synthesize different amounts of PAB. The most resistant strains produced the highest amounts. Furthermore, Landy *et al.* (6) pointed out that they were unable to detect any significant difference in the production of PAB by sulphonamide-susceptible and resistant strains of *Escherichia coli, Shigella dysenteriae, Vibrio cholera* and *Diplococcus pneumoniae,* Types I, II and III.

Strains resistant to sulpha drugs were obtained from Dr. Wesley Spink of the Medical School, University of Minnesota. These strains of *Staph. aureus* 7c, 14c, 117, 605, 610 and 620, as noted in Table I, are also resistant to citrinin.

Taking into consideration the fact that the addition of PAB to the assay medium does not interfere with the bacteriostatic ability of citrinin, and in view of the resistance to citrinin of the sulpha drug-fast strains of *Staph. aureus,* it may be suggested that the mechanism of resistance of these strains is expressed not only in the ability to produce a sufficient amount of PAB, but apparently involves other factors. To explain this mechanism of resistance to citrinin, further research is necessary.

Summary

During the course of investigation on potency of citrinin *in vitro* it was found that citrinin exerts bacteriostatic activity on gram-positive organisms only. Assay media containing 1 per cent glucose demonstrated higher values of potency of citrinin than plain media. It was also demonstrated that citrinin obtained by different methods of purification differed in bacteriostatic potencies.

Addition of fresh horse serum (5 per cent) to assay media resulted in reduction of the bacteriostatic potency of citrinin, whereas p-aminobenzoic acid did not interfere with it.

The effect of glucose on the bacteriostatic potencies of antibiotic substances and the mechanism of resistance of bacteria to the antibiotic substances are also discussed.

Toxicity tests of citrinin *in vivo* revealed that two mgs. of citrinin proved to be lethal to 20 gm. mice, whereas 50 mg. per kilogram body weight in rats resulted in no ill effect to the animals.

Acknowledgment

The authors are indebted to Dr. W. Spink for sulphonamide-resistant strains of *Staph. aureus,* to Dr. R. L. Noble for making toxicity tests of citrinin *in vivo*

and to Drs. S. A. Waksman and E. T. Bynoe for tests of citrinin against some organisms, *in vitro*. The authors also wish to express their appreciation to Dr. A. G. Lochhead, Dominion Agricultural Bacteriologist, for advice during the course of this work.

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Canadian Journal of Public Health

DISTRIBUTION OF PENICILLIN FOR CIVILIAN USE IN CANADA

LAST May the production of penicillin in the United States reached proportions which permitted a limited distribution to hospitals for the treatment of civilians. Shortly after, the requirements of the Army and Navy increased greatly and it was with difficulty that the quota for civilian hospitals was maintained. In Canada the entire supply of penicillin from the three plants engaged in its production—two of which were established by the Dominion Government—has been continuously required by the Armed Services. Early in July distribution for civilian use was commenced in Canada through the co-operation of the War Production Board in Washington which made available a supply of penicillin from United States manufacturers. Penicillin was offered to all public general hospitals on a monthly quota basis. Smaller hospitals were permitted to obtain penicillin when needed and provision was made to permit of the treatment of patients outside of hospitals under certain emergencies. Responsibility for the distribution of penicillin in Canada was placed with the office of the Controller of Chemicals, Department of Munitions and Supply; and a Medical Advisory Committee was appointed to confer with the Controller in all matters relating to the distribution and use of penicillin. A "Guide for Penicillin Treatment,"[1] issued by the Committee, was furnished to hospitals when the distribution of penicillin was first undertaken and has formed the basis for the use of the limited quantities of penicillin available. The National Drug and Chemical Company of Canada provided their facilities without charge, so that stocks of penicillin were accessible in centres across Canada. In the United States the price of penicillin as supplied by the different manufacturers varies. In Canada, however, the Controller of Chemicals established a uniform price for the product. This action is to be commended, as varying prices would have occasioned dissatisfaction among hospitals receiving supplies.

On September 15th the total number of general hospitals placed on the roster to receive a regular monthly quota of penicillin exceeded six hundred—almost double the number in July. In addition, sanatoria, mental hospitals, and certain private hospitals were furnished with regular supplies. The initial price

[1]*See page 377 of this issue.*

of $6.00 per 100,000 units has been reduced to $4.50. Canadian production at present is three times as great as it was last June, and it is likely that in six months the output will be double what it is today.

The distribution of penicillin for civilian use has been well handled, and many physicians can speak of the thoroughness with which their enquiries have been dealt and the speed with which supplies have been made available for the treatment of conditions listed by the Medical Advisory Committee. Mr. E. T. Sterne, Controller of Chemicals, his staff, and the Medical Advisory Committee deserve high commendation for providing such an effective service.

THE ANNUAL MEETING

THE Canadian Public Health Association will hold its thirty-third annual meeting with the Ontario Health Officers Association in the Royal York Hotel, Toronto, on November 6th to 8th. This year's meeting should do much to stimulate Canadian public-health workers to plan for the post-war period. One session will focus attention on international public health and the part Canada must play. Dr. Melville MacKenzie, of the British Ministry of Health, who was recently named Medical Director of UNRRA in Europe, and Dr. James A. Crabtree, Deputy Director, Division of Health, UNRRA, will speak of the world task that faces public health. One of Britain's leaders in public health, Dr. George F. Buchan, who is well known to members of the Association, will discuss Britain's new social-security program. Many speak of this plan as the greatest social-security charter ever introduced by any government in any country. The Association will be honoured also in having a number of distinguished leaders from the United States, including Dr. Felix J. Underwood, Executive Officer of the Mississippi State Board of Health and Past President of the American Public Health Association; Dr. Reginald M. Atwater, Executive Secretary of the American Public Health Association; Dr. John A. Ferrell, who was recently appointed Medical Director of The John and Mary R. Markle Foundation, New York; Dr. W. A. McIntosh, of the International Health Division of The Rockefeller Foundation; and Miss Dorothy Deming, formerly Director of The National Organization for Public Health Nursing and internationally recognized as an authority in public-health nursing. The Honourable R. P. Vivian, M.D., Minister of Health and Welfare for the Province of Ontario, and Honorary President of the Canadian Public Health Association, will be the principal speaker at the annual dinner. During the meetings the forward program of public health in the various provinces will be outlined, including the developments in health insurance in Manitoba as presented by the Honourable Ivan Schultz, Minister of Health and Public Welfare; the extension of public-health services in Ontario; services provided under the Maternity Hospitalization Act of Alberta; and further progress in the control of tuberculosis in Quebec and in other provinces.

Thirty-Third Annual Meeting

CANADIAN PUBLIC HEALTH ASSOCIATION

AND

Twenty-Ninth Annual Meeting

ONTARIO HEALTH OFFICERS ASSOCIATION

ROYAL YORK HOTEL, TORONTO

NOVEMBER 6, 7 AND 8, 1944

DIRECTORY OF SESSIONS

Monday, November 6th

8.30 a.m.—Registration—Members of the Ontario Health Officers Association are also members of the Canadian Public Health Association. As this is a joint conference, it is requested that they register. The registration fee is $1.00. CONVENTION FOYER.

9.30 a.m.—Ontario Health Officers Association. BANQUET HALL.

Canadian Public Health Association. Section Meetings:
Epidemiology. HALL C.
Public Health Nursing. HALL D.

12.30 p.m.—Canadian Public Health Association and Ontario Health Officers Association. Luncheon. TUDOR ROOM. Tickets, $1.25.

2.15 p.m.—Canadian Public Health Association and Ontario Health Officers Association. First General Session. BANQUET HALL.

Canadian Public Health Association. Section of Service Hygiene. HALL B.

8.15 p.m.—Canadian Public Health Association and Ontario Health Officers Association. Special Session: Public Health in the Post-war World. BANQUET HALL.

Tuesday, November 7th

9.00 a.m.—Ontario Health Officers Association. BANQUET HALL.

Ontario Health Officers Association:
Veterinary Inspection Services Section. HALL D.

Canadian Public Health Association. Section Meetings:
Epidemiology. HALL C.
Service Hygiene. HALL B.

12.30 p.m.—Canadian Public Health Association. Luncheon and Business Meeting of the Executive Council. HALL A. Tickets $1.25.

2.15 p.m.—Canadian Public Health Association and Ontario Health Officers Association. Second General Session. BANQUET HALL.

6.30 p.m.—Canadian Public Health Association and Ontario Health Officers Association. Dinner. BALLROOM. Tickets, $2.00.

Wednesday, November 8th

9.00 a.m.—Ontario Health Officers Association. BANQUET HALL.
Canadian Public Health Association. Section Meetings:
Epidemiology and Administration. HALL C.
Public Health Nursing. CLUB ROOM.
Service Hygiene. HALL D.

2.15 p.m.—Canadian Public Health Association and Ontario Health Officers Association. Third General Session. BANQUET HALL.

GENERAL INFORMATION

Registration. All delegates and guests are expected to register. A fee of $1.00 is charged to meet in part the expenses of the conference. Registration Desk: CONVENTION FOYER.

The scientific sessions, the annual dinner, and the luncheon sessions will begin promptly at the hour indicated. Members can assist by planning their schedule in advance and by being on time. If you are planning to attend the dinner or the luncheons, **please buy your tickets well in advance.** The accommodation is limited.

The annual dinner of both Associations will be held in the BALLROOM on Tuesday, November 7th, at **6.30 p.m.** The speaker will be the Hon. R. P. VIVIAN, M.D., Minister of Health and Welfare for the Province of Ontario. Greetings from the American Public Health Association will be extended by Dr. FELIX S. UNDERWOOD, Executive Officer, Mississippi State Board of Health, and Retiring President of the Association. Tickets ($2.00) will be on sale at the Registration Desk from Monday, November 6th. **Early reservations are desirable, as the accommodation is limited to 250.**

A luncheon of both Associations will be held in the TUDOR ROOM on Monday, November 6th, **12.30 p.m.** The speaker will be Dr. GEORGE F. DAVIDSON, Executive Director of the Canadian Welfare Council, Ottawa. Tickets ($1.25) will be on sale at the Registration Desk from **8.30 a.m.** Monday. The accommodation is limited to 125.

Exhibits. The attention of members is directed to the exhibits of the following companies, which will be on view in the CONVENTION FOYER:

Abbott Laboratories Limited
Anglo Canadian Drug Company
The British Drug Houses (Canada) Ltd.
Burroughs Wellcome & Co.
Ferranti Electric Limited
Charles E. Frosst & Co.
The J. F. Hartz Co. Ltd.
Ingram & Bell Limited
Lederle Laboratories, Inc.
Proctor & Gamble Co. of Canada, Ltd.
Reckitt & Colman (Canada) Limited
The Ryerson Press
The Upjohn Company
William R. Warner & Co. Ltd.
Winthrop Chemical Company, Inc.
G. H. Wood & Co. Limited
John Wyeth & Brother (Canada) Ltd.

In addition, scientific exhibits will be provided by the Department of Health of Ontario; the Division of Nutrition, Department of Pensions and National Health, Ottawa; the Victorian Order of Nurses, and the Health League of Canada.

TENTATIVE PROGRAM

The program presented in the following pages is necessarily incomplete and subject to change, but offers a preview of the sessions planned for this year's annual meetings.

Monday, November 6th - 9.30 a.m.

ONTARIO HEALTH OFFICERS ASSOCIATION

FIRST SESSION—BANQUET HALL

Problems in Environmental Sanitation

Dr. A. E. BERRY, Director, Division of Sanitary Engineering, Department of Health, and Staff.

Venereal-Disease Control at the Municipal Level

Major J. A. LEROUX, R.C.A.M.C., Director, Division of Venereal-Disease Control, Staff, and others.

Monday, November 6th - 9.30 a.m.

CANADIAN PUBLIC HEALTH ASSOCIATION

Section of Epidemiology

HALL C

Cases of Exposure to Methyl Bromide Vapors

DR. F. J. TOURANGEAU and MR. SARTO R. PLAMONDON, M.S., C.E., Division of Industrial Hygiene, Ministy of Health and Social Welfare, Quebec.

Services Provided under the Maternity Hospitalization Act of Alberta

Dr. MALCOLM R. BOW, Deputy Minister of Health, Province of Alberta.

Milk Control under a Board of Public Utilities

Dr. J. S. ROBERTSON, Director of the Western Health Unit, Department of Public Health of Nova Scotia.

Report of a Tuberculosis Survey among Ottawa Federal Civil Servants

Dr. S. A. HOLLING, Clinician, Division of Tuberculosis Prevention, Department of Health of Ontario, Toronto.

The Control of Tuberculosis in Montreal

Dr. LEO LADOUCEUR, Chief, Division of Tuberculosis, Department of Health, Montreal, Quebec.

Monday, November 6th - 9.30 a.m.

CANADIAN PUBLIC HEALTH ASSOCIATION
Public Health Nursing Section

HALL D

Chairman: Miss HELEN G. MCARTHUR, Director of Public Health Nursing, Province of Alberta.

Business Session:

Report of the Study Committee, Miss MARY S. MATHEWSON, Convener.
Reports of interest from the Provinces.

History and Activities of the Health Committee in the Town of Picton, Ontario

Mrs. WM. HAGGART, B.A., Public Health Nurse, Picton.

Report on the Salary Schedule recently drawn up in British Columbia as it affects public health nurses; and on the increase in the venereal-disease control program of public health nurses

MISS DOROTHY E. TATE, Acting Director of Public Health Nursing, Provincial Board of Health, Victoria, B.C.

Monday, November 6th - 12.30 p.m.

CANADIAN PUBLIC HEALTH ASSOCIATION
and
ONTARIO HEALTH OFFICERS ASSOCIATION

LUNCHEON—TUDOR ROOM

Tickets ($1.25) will be on sale at the Registration Desk from **8.30 a.m.** Monday. Early reservations are desirable, as the accommodation is limited to 150.

Address:

Dr. George F. DAVIDSON, Executive Director of the Canadian Welfare Council, Ottawa.

Presentation of the awards in the 1943 National Health Honour Roll, conducted by the Canadian Public Health Association and the American Public Health Association, with the financial assistance of the W. K. Kellogg Foundation and the Metropolitan Life Insurance Company.

Dr. REGINALD M. ATWATER, Executive Secretary of the American Public Health Association, New York, will present plaques to the medical officers of the winning cities and counties:

Hamilton, Ontario—Dr. J. E. DAVEY, Medical Officer.
St. Boniface, Manitoba—Dr. PAUL L'HEUREUX.
St. Catharines, Ontario—Dr. D. V. CURREY.
Windsor, Ontario—Dr. JOHN HOWIE.
Arthabaska County, Quebec—Dr. EMILE POISSON.
Nicolet County, Quebec—Dr. A. LAPERRIERE.
Okanagan Valley Health Unit, British Columbia—Dr. J. M. HERSHEY.
St. Hyacinthe-Rouville Counties, Quebec—Dr. J. MARC BERGERON.
St. James-St. Vital Health Unit, Manitoba—Dr. I. M. CLEGHORN.
St. Jean-Iberville-Laprairie-Napierville Counties, Quebec—Dr. A. LAPIERRE.
Shefford County, Quebec—Dr. R. F. BRUNEAU.

Monday, November 6th - 2.15 p.m.

CANADIAN PUBLIC HEALTH ASSOCIATION
and
ONTARIO HEALTH OFFICERS ASSOCIATION

FIRST GENERAL SESSION—BANQUET HALL

Presidential Address

Dr. B. T. McGhie, Deputy Minister of Health and Hospitals, Province of Ontario, and President of the Canadian Public Health Association.

Some Problems in Tuberculosis

Dr. G. C. Brink, Director, Division of Tuberculosis Prevention, Department of Health of Ontario, Toronto.

Putting Merit into Merit Systems

Dr. Reginald M. Atwater, Executive Secretary, The American Public Health Association, New York.

Public Treatment Services for Venereal Infection

Lieut.-Col. D. H. Williams, R.C.A.M.C., Chief, Division of Venereal-Disease Control, Department of Pensions and National Health, Ottawa.

The Dominion Housing Program

Mr. F. W. Nicolls, Director of Housing, National Housing Administration, Ottawa.

Monday, November 6th - 2.15 p.m.

CANADIAN PUBLIC HEALTH ASSOCIATION
Section of Service Hygiene

HALL B

Monday, November 6th - 8.15 p.m.

CANADIAN PUBLIC HEALTH ASSOCIATION
and
ONTARIO HEALTH OFFICERS ASSOCIATION

SPECIAL SESSION—BANQUET HALL

Public Health in the Post-War World.

Recent Developments in the Field of International Collaboration in Medicine

Dr. Melvile MacKenzie, Ministry of Health, London.
Dr. James A. Crabtree, Deputy Director, Division of Health, United Nations Relief and Rehabilitation Administration, Washington.

Britain's Health in Wartime

Dr. George F. Buchan, Medical Officer of Health, Borough of Willesden, Kilburn, London.

Tuesday, November 7th - 9.00 a.m.

ONTARIO HEALTH OFFICERS ASSOCIATION

SECOND SESSION—BANQUET HALL

A Broader Program of Public Health for Ontario

Sanitation (Post-war)
Dr. A. E. BERRY, Director, Division of Sanitary Engineering.

General Principles of the Program as Proposed
The Hon. R. P. VIVIAN, M.D., Minister of Health.

Administrative Procedures
Dr. J. T. PHAIR, Chief Medical Officer of Health.

Venereal-Disease Control
Major J. A. LEROUX, R.C.A.M.C., Director, Division of Venereal-Disease Control.

Industrial Hygiene
Dr. J. G. CUNNINGHAM, Director, Division of Industrial Hygiene.

Tuesday, November 7th - 9.00 a.m.

ONTARIO HEALTH OFFICERS ASSOCIATION
Veterinary Inspection Services Section

HALL D

Tuesday, November 7th - 9.00 a.m.

CANADIAN PUBLIC HEALTH ASSOCIATION
Section of Epidemiology

HALL C

Medical Examination of Employees in Hotels, Restaurants and Other Refreshment Places
Dr. ARTHUR WILSON, Medical Health Officer, Saskatoon.

Acute Methyl Alcohol Poisoning—Observations in Some Thirty Cases
Dr. ARNOLD BRANCH, Director, Bureau of Laboratories, Department of Health of New Brunswick, and Dr. D. J. TONNING, Attending Physician, Saint John General Hospital, Saint John.

A Few Aspects of the Venereal-Disease Control Program in the Province of Quebec
DR. DAVID BEAULIEU, Director, Division of Venereal Diseases, Ministry of Health and Social Welfare, Province of Quebec, Montreal.

The Diphtheria Situation in Montreal
Dr. C. A. BOURDON, Director of Health Districts, Department of Health of Montreal.

An Appraisal of the Efficiency of Diphtheria Toxoid after an Interval of Five Years
Dr. C. J. W. BECKWITH and Dr. M. R. MACDONALD, Cape Breton Island Health Unit, Department of Public Health of Nova Scotia.

Tuesday, November 7th - 9.00 a.m.

CANADIAN PUBLIC HEALTH ASSOCIATION
Section of Service Hygiene

HALL B

Tuesday, November 7th - 12.30 p.m.

CANADIAN PUBLIC HEALTH ASSOCIATION
Luncheon and Business Meeting of the Executive Council

HALL A. (Tickets $1.25)

Chairman: Dr. B. T. McGHIE, Deputy Minister of Health and Hospitals, Province of Ontario, and President of the Canadian Public Health Association.

Presentation of reports.

Plans for 1945.

Tuesday, November 7th - 2.15 p.m.

CANADIAN PUBLIC HEALTH ASSOCIATION
and
ONTARIO HEALTH OFFICERS ASSOCIATION

SECOND GENERAL SESSION—BANQUET HALL

Mental-Hygiene Provisions in Public-Health Programs
Dr. CLARENCE M. HINCKS, General Director, The National Committee for Mental Hygiene (Canada), Toronto.

Tuberculosis Control
Dr. W. H. HATFIELD, Director, Division of Tuberculosis Control, Provincial Board of Health of British Columbia, Vancouver.

Tuberculosis Control in the Army
Colonel J. D. ADAMSON, R.C.A.M.C., Consultant in Medicine, Department of National Defence, Ottawa.

How Manitoba Expects to Implement Health Insurance.
The Hon. IVAN SCHULTZ, Minister of Health and Public Welfare, Province of Manitoba, Winnipeg.

Housing Problems in Wartime:
In Vancouver - - Dr. STEWART MURRAY, Senior Medical Health Officer.
In Edmonton - - Dr. G. M. LITTLE, Medical Officer of Health.
In Windsor - - - Dr. JOHN HOWIE, Medical Officer of Health.

Tuesday, November 7th - 6.30 p.m.

CANADIAN PUBLIC HEALTH ASSOCIATION
and
ONTARIO HEALTH OFFICERS ASSOCIATION

ANNUAL DINNER—BALLROOM

Tickets ($2.00) will be on sale at the Registration Desk from **8.30 a.m.** Monday. Early reservations are advisable as the accommodation is limited to 250.

Chairman: Dr. B. T. McGHIE, Deputy Minister of Health and Hospitals, Province of Ontario, and President of the Canadian Public Health Association.

Greetings from the American Public Health Association
Dr. FELIX J. UNDERWOOD, Executive Officer, Mississipi State Board of Health, and Retiring President of the American Public Health Association.

Address
The Hon. R. P. VIVIAN, M.D., Minister of Health and Welfare, Province of Ontario, and Honorary President of the Canadian Public Health Association.

Wednesday, November 8th - 9.00 a.m.

ONTARIO HEALTH OFFICERS ASSOCIATION

SECOND SESSION—BANQUET HALL

Interpretation of Public Health Nursing Services
Miss EDNA L. MOORE, Director, Division of Public Health Nursing

The Newer Concept of Public Health Dentistry
DR. HARVEY W. REID, Chairman, Executive Committee, Board of the Royal College of Dental Surgeons, Toronto.

The Ontario Municipal Health Services Act
Dr. K. G. GRAY, Assistant Deputy Minister of Health.

The Control of Rabies
Dr. W. MOYNIHAN, District Veterinary Inspector, Health of Animals Branch, Dominion Department of Agriculture, Toronto; and Dr. A. L. MACNABB, Director, Division of Laboratories, Department of Health of Ontario, Toronto.

Wednesday, November 8th - 9.00 a.m.

CANADIAN PUBLIC HEALTH ASSOCIATION
Epidemiology and Public Health Administration

HALL C

A New Pattern in Registration Concepts
Mr. J. T. MARSHALL, Chief, Vital Statistics Branch, Dominion Bureau of Statistics, Ottawa.

The Need for Planning Now for Child and Maternal Hygiene in the Post-war Period
Dr. ERNEST COUTURE, Chief, Division of Maternal and Child Hygiene, Department of Pensions and National Health, Ottawa.

Recording the Child-Hygiene Program in Calgary
Dr. W. H. HILL, Medical Officer of Health, Calgary.

An Outbreak of Typhoid Fever due to Cheese
Mr. D. B. MENZIES, Provincial Sanitary Engineer, Edmonton, Alberta.

A Cheese-Borne Outbreak of Typhoid Fever, 1944
DR. A. R. FOLEY, Epidemiologist, Ministry of Health and Social Welfare, Quebec; and DR. E. POISSON, Medical Officer of Health, County Health Unit, Victoriaville, Que.

Wednesday, November 8th - 9.00 a.m.

CANADIAN PUBLIC HEALTH ASSOCIATION
Section of Service Hygiene

HALL D

Wednesday, November 8th - 9.00 a.m.

CANADIAN PUBLIC HEALTH ASSOCIATION
Public Health Nursing Section

CLUB ROOM

Chairman: Miss HELEN G. MCARTHUR, Director of Public Health Nursing, Province of Alberta.

Report of the Committee on Post-War Planning, Canadian Nurses Association—including UNRRA
Miss E. A. ELECTA MACLENNAN, Secretary, Committee on Post-War Planning, Canadian Nurses Association, Montreal.

Open Discussion:

Personnel Policies as applied to Canada.

The Public Health Nurse in Health-Insurance Plans.

The Development of the Venereal-Disease Program.

Ways and Means of Meeting the Shortage of Trained Personnel.

Wednesday, November 8th - 2.15 p.m.

CANADIAN PUBLIC HEALTH ASSOCIATION
and
ONTARIO HEALTH OFFICERS ASSOCIATION

THIRD GENERAL SESSION—BANQUET HALL

Personnel Policies and Practices in Public Health Nursing
MISS DOROTHY DEMING, Consultant in Public Health Nursing, New York.

Penicillin
Dr. P. H. GREEY, Department of Pathology and Bacteriology, University of Toronto.

Nutrition and Public Health
Dr. L. B. PETT, Chief, Division of Nutrition, Department of Pensions and National Health, Ottawa.

Britain's New Social-Security Program
Dr. GEORGE F. BUCHAN, Medical Officer of Health, Borough of Willesden, Kilburn, London.

CANADIAN INSTITUTE OF SANITARY INSPECTORS
(Ontario Branch)

ANNUAL MEETING

ROYAL YORK HOTEL, TORONTO

November 6, 7 and 8, 1944

President: R. M. MacPherson, B.A., C.S.I.(C.)

Monday, November 6th

PRIVATE DINING ROOM No. 10

9.00 a.m.—Registration.

10.00 a.m.—President's Welcome.

10.15 a.m.—Dairy Farm Inspection
J. E. Weis, C.S.I.(C.), Department of Health, Stratford, Ontario.

11.00 a.m.—Housing
F. Austin, Department of Health, Winnipeg, Manitoba.

2.00 p.m.—Hygiene Problems in an Occupied Town
Lieut.-Col. P. A. Scott, Officer Commanding, School of Military Hygiene, R.C.A.M.C., Camp Borden, Ontario.

3 30 p.m.—The Medical Officer and Cyanide Fumigation
D. V. Currey, M.D., D.P.H., Medical Officer of Health, St. Catharines.

Tuesday, November 7th

PRIVATE DINING ROOM No. 10

9.30 a.m.—Diseases Communicable to Man from Animals
Marcel Picard, M.V., C.S.I.(C.), Ministry of Health, Province of Quebec.

11.00 a.m.—Rural Sanitation
A. E. Berry, M.A.Sc., C.E., Ph.D., Director, Division of Sanitary Engineering, Department of Health of Ontario, Toronto.

12.15 p.m.—Luncheon. LIBRARY.
Guest Speaker: C. D. McGilvray, V.S., M.D.V., D.V.Sc., Principal, Ontario Veterinary College, Guelph, Ont.

2.00 p.m.—Annual Meeting.

Wednesday, November 8th

PRIVATE DINING ROOM No. 10

9.30 a.m.—Simplifying the Demonstration of Equipment Sanitation
Morley C. Jameson, B.S.A., M.Sc., Assistant Professor of Bacteriology, University of Manitoba, Winnipeg.

11.00 a.m.—The Role of the Sanitary Inspector in an Approved Public Health Service
John T. Phair, M.B., D.P.H., Chief Medical Officer of Health, Department of Health of Ontario, Toronto.

2.00 p.m.—The Sanitary Inspector and Swimming Pools
R. F. Heath, A.C.I.C., Chief Chemist, Department of Public Health, Toronto.

3.00 p.m.—Round-Table Discussion and Question Box.